

MPS I Intrathecal ERT for Spinal Cord Compression

One Year Extension Study Approved

Enzyme replacement therapy (ERT) has been developed for mucopolysaccharidosis I (MPS I), a lysosomal storage disorder. ERT helps many physical ailments due to the disease, but does not treat the central nervous system, due to inability to cross the blood brain barrier. The purpose of this study is to test delivery of ERT to the spinal fluid via intrathecal injection in patients with MPS I. In this pilot study, recombinant human α -L-iduronidase will be administered intrathecally once per month for four months to individuals age 8 and older with the Hurler-Scheie and Scheie forms of MPS I and spinal cord compression. For questions regarding age, please contact Dr. Dickson. If successful, intrathecal delivery could represent a practical, straightforward method of treating central nervous system disease due to lysosomal storage.

Primary Outcomes: safety of intrathecal enzyme treatment by blood and spinal fluid tests each month; improvement in neurologic signs related to spinal cord compression, by neurologic examination and Japanese Orthopedic Association Scale each month; improvement in neurologic symptoms related to spinal cord compression, by subjective assessments and independence of functioning scale each month; improvement in mobility, by six-minute walk test each month; improvement in spinal cord compression by MRI imaging and somatosensory evoked potentials at baseline and 4 months; improvement in lysosomal storage by spinal fluid glycosaminoglycan levels at each treatment. Secondary Outcomes: improvement in spinal fluid pressure, by opening pressure measurements at each intrathecal treatment; improvement in hydrocephalus and other brain lesions by MRI at baseline and 4 months

Expected Total Enrollment: 10

Additional information can be obtained at

<http://www.clinicaltrials.gov/ct/show/NCT00215527?order=1> or by contacting the Principal Investigator, Dr. Patricia Dickson, 310-222-4145 pdickson@ucla.edu

MPS I Intrathecal ERT for Children Being Considered for Transplantation

The University of Minnesota has recently obtained FDA approval for the delivery of Laronidase into the spinal fluid of children with Hurler syndrome being considered for marrow/cord blood transplantation. The goal of these studies is to decrease the neuropsychologic decline that has been observed in children with Hurler from the time the patients are initially evaluated to the time they are 1 year from transplantation. The hypothesis is that there is a significant delay in achieving sufficient enzyme levels in the brain following transplantation, and that this may be overcome by giving enzyme into the spinal fluid until this occurs. Patients with Hurler syndrome that are between 8 and 36 months of age that have not previously received enzyme therapy and are being considered for transplantation at the University of Minnesota are eligible. Patients receiving Laronidase in the spinal fluid will also be on intravenous Laronidase prior to transplant. The study will involve 4 doses of Laronidase given during a lumbar puncture (LP, or spinal tap) approximately 3 months before transplantation, at the time of

admission to the hospital for the transplant, 3 months after the transplant and 6 months after the date of the transplant. The Principal Investigator of the study is Dr. Paul Orchard, who can be reached at 612-626-2961, or by email at orcha001@umn.edu. Alternatively, Teresa Kivisto is the nurse coordinator involved with this study, and she can be reached at 612-273-2924, or by email at TKIVIST1@Fairview.org.

MPS II

Shire Human Genetic Therapies is committed to conducting a clinical trial in individuals with MPS II who have neurological involvement. Currently, this study is projected to be at the University of North Carolina, and details regarding inclusion criteria and study design are forthcoming. For more information, please contact Amy Fisher at Shire Human Genetic Therapies (919-468-0646; afisher@shire.com)

MPS III

Shire Pharmaceuticals Group as part of their research to evaluate new approaches to the problem of treatment of the central nervous system, is hoping to move their MPS III-A program forward. If the trial to directly administer the enzyme into the central nervous system of individuals with MPS II is successful, they hope to expand their research initiatives to include MPS III-A. The Shire website is www.shire.com.

MPS IV

The Carol Ann Foundation and International Morquio Organization announced in 2005 that the Swiss company, Vivendy (formerly Inotech) will start a Natural History study in late 2008 in 4-5 international centers. They plan to start a clinical therapy study in the next 24 months. They are encouraging families to enroll their children in the MPS IV registry, or if already enrolled, to update the information yearly, www.morquio.com. This natural history information is critical for drug development and follow-up. For more information, contact Mary Smith, President of the Carol Ann Foundation and International Morquio Organization, 520.744.2531, mbs85705@yahoo.com.

In June 2008 BioMarin announced their program for MPS IVA that has been in development the last two years. Their first of several studies is a treatment study that will involve 15-20 patients in 1-3 sites in one or two countries, and that will involve patients receiving escalating doses of enzyme via a weekly IV infusion over a period of about 36 weeks. They will also be conducting a Morquio Clinical Assessment Program or MorCAP that will involve about 15 centers in many countries and will evaluate the disease situation for patients globally. Finally they expect to have a Phase 3 double-blind placebo controlled study that might include 50-100 patients from many centers. Being in the MorCAP program will improve a patient's chances of being in the Phase 3. Additional information can be found at www.morquioBMRN.com.

MPS VII

A gene therapy clinical trial for mucopolysaccharidosis type VII (MPS VII), also known as Sly Syndrome has been put on hold pending additional data.

ML II/III

There currently are no programs in place for developing treatment options for ML II/III